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Therapeutic Class Review
Intranasal Corticosteroids

Overview/Summary

Intranasal corticosteroids are primarily used to treat allergic rhinitis and may be useful in the treatment of some forms of nonallergic rhinitis.[1] Symptoms typically associated with allergic rhinitis include nasal congestion, rhinorrhea, sneezing, and/or nasal itching. These symptoms result from a complex allergen driven mucosal inflammation caused by interplay between resident and infiltrating inflammatory cells and a number of vasoactive and proinflammatory mediators.[1] Intranasal corticosteroids downregulate the inflammatory response by binding to the glucocorticosteroid receptors of inflammatory cells and causing a conformational change, thereby controlling the rate of protein synthesis and suppressing the transcription of cytokine and chemokine genes.[2]

Continuous administration of intranasal corticosteroids is more efficacious than as-needed dosing and the onset of therapeutic effect occurs between three and twelve hours.[1] When administered at recommended doses, intranasal corticosteroids are not generally associated with any clinically significant systemic side effects. The most common side effects include nasal irritation and mild epistaxis.[3] Due to both the route of administration and the relatively low systemic bioavailability of these agents, drug interactions are limited.

Two currently available intranasal corticosteroids, beclomethasone and mometasone, are also Food and Drug Administration (FDA) approved for the treatment of nasal polyps.[4,5] Nasal polyposis is an inflammatory condition of the nasal and sinus mucosa and usually presents as persistent nasal obstrutction.[1] Intranasal corticosteroids improve sense of smell and reduce nasal congestion. Intranasal beclomethasone is used principally to prevent recurrence of nasal polyps following surgical removal.[4]

Beclomethasone and fluticasone propionate are also FDA approved for the management of nonallergic rhinitis.[4,6] Examples of nonallergic rhinitis include infectious rhinitis, hormonal rhinitis, vasomotor nonallergic rhinitis with eosinophilia syndrome (NARES). Unlike allergic rhinitis; nonallergic rhinitis is characterized by periodic or perennial symptoms that are not a result of immunoglobulin E-dependent events.

Flunisolide and fluticasone propionate are the only two intranasal corticosteroids currently available in a generic nasal spray formulation.

According to the current clinical guidelines on the management of rhinitis, treatment should consist of patient education, allergen avoidance activities, and pharmacological therapies. Patients should be educated on how to avoid known triggers, such as aeroallergens, dust mites, molds and irritants, whenever possible. In addition to environmental control measures, pharmacological therapies may be used to control symptoms. Intranasal corticosteroids should be considered first-line therapy in patients with moderate to severe allergic rhinitis.[1,3] The combination of an antihistamine and a leukotriene inhibitor is more effective than either therapy alone, however, the combination is not more efficacious than treatment with intranasal corticosteroids.[1] Additionally, intranasal anticholinergics have increased efficacy for the management of rhinorrhea when used in combination with intranasal corticosteroids.

Medications

Table 1. Medications Included Within Class Review

Generic Name (Trade name)	Medication Class	Generic Availability
Beclomethasone (Beconase AQ®)	Intranasal corticosteroid	-
Budesonide (Rhinocort Aqua®)	Intranasal corticosteroid	-
Ciclesonide (Omnaris®)	Intranasal corticosteroid	-
Flunisolide (Nasarel®)	Intranasal corticosteroid	✔
Fluticasone furoate (Veramyst®)	Intranasal corticosteroid	-
Fluticasone propionate (Flonase®)	Intranasal corticosteroid	✔
Mometasone (Nasonex®)	Intranasal corticosteroid	-
Triamcinolone (Nasacort AQ®)	Intranasal corticosteroid	-

Indications

Table 2. Food and Drug Administration Approved Indications[4-11]

Generic Name	Nasal Polyps	Nonallergic (Vasomotor) Rhinitis	Perennial Allergic Rhinitis	Seasonal Allergic Rhinitis
Beclomethasone	✔	✔	✔	✔
Budesonide			✔	✔
Ciclesonide			✔	✔
Flunisolide			✔	✔
Fluticasone furoate			✔	✔
Fluticasone propionate		✔	✔	✔
Mometasone	✔		✔	✔
Triamcinolone			✔	✔

Pharmacokinetics

Table 3. Pharmacokinetics[12]

Generic Name	Onset of Action (hours)	Duration	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Beclomethasone	72	Not reported	10-15	Beclomethasone-17-monopropionate	3.0 (2.8*)
Budesonide	10-24	Not reported	60	None	2-3
Ciclesonide	Not reported	Not reported	<20	Des-ciclesonide	Not specified
Flunisolide	72	Not reported	50	6-beta-hydroxylated metabolite	1.0-2.0 (3.2-4.6*)
Fluticasone furoate	12	Not reported	Not reported	None	15.1
Fluticasone propionate	12	Not reported	<5	None	7.2
Mometasone	24	Not reported	Not reported	None	5.8
Triamcinolone	24	Not reported	Extensive	None	2-3

*Value for metabolite.

Clinical Trials

Numerous clinical trials have demonstrated the efficacy and safety of intranasal corticosteroids in the treatment of both perennial and seasonal allergic rhinitis, and non allergic rhinitis. Daily administration of intranasal corticosteroids, improved both total nasal symptom and health related quality of life scores in patients with rhinitis and therapy was well tolerated. In addition, numerous head-to-head clinical trials have demonstrated no significant clinical differences among the currently available intranasal corticosteroids and all agents within the class should be considered equally efficacious.[13-38]

Differences in sensory perceptions and patient preference of one agent over another have been noted in a few clinical trials.[34,39-43] Patients administering the agents noted differences in odor, aftertaste, and severity of irritation, however, these differences do not result in improved outcomes.

Specifically, head-to-head trials evaluating the efficacy and safety of fluticasone propionate and flunisolide, demonstrate these agents are comparable to other agents within the class.[20,22-30,33,36-38] In one study, treatment with fluticasone propionate resulted in significantly less nasal blockage (P=0.002), nasal discharge (P=0.002), and eye watering/irritation (P=0.048) compared to treatment with beclomethasone.[27] In a second study, fluticasone propionate reduced patient-rated nasal symptom scores significantly better than beclomethasone at all time points measured (P<0.05).[28] However, additional results of these studies reinforce that all of the intranasal corticosteroids should be considered equally efficacious.

The two most recently Food and Drug Administration (FDA) approved intranasal corticosteroids, ciclesonide and fluticasone furoate, have been shown to be superior to placebo in the treatment of allergic rhinitis. In a long-term efficacy and safety trial evaluating the efficacy of ciclesonide compared to placebo, reductions from baseline in 24 hour reflective total nasal symptoms scores (rTNSS) were significantly greater in the ciclesonide group (P<0.0001).[44] In addition, treatment with ciclesonide produced a greater improvement in combined Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores (P=0.04). No head-to-head trials have been conducted comparing ciclesonide to other agents within the class.

In two clinical trials evaluating the efficacy of fluticasone furoate compared to placebo, daily administration of fluticasone furoate resulted in a significant decrease from baseline in rTNSS (P<0.001, P<0.001), morning predose instantaneous total nasal symptom scores (iTNSS) (P<0.001, P<0.001), and reflective total ocular symptom scores (rTOSS) (P<0.0001, P=0.004).[45,46] In addition, patients treated with fluticasone furoate reported significant improvements in the overall RQLQ scores compared to patients treated with placebo (P<0.001, P<0.001). In one study, the most common side effects reported by patients treated with fluticasone furoate included headache and epistaxis.[46] Currently there have been no head-to-head studies conducted comparing fluticasone furoate to other agents within the class and in the absence of published direct comparison clinical trials; it is unclear whether there is a therapeutic advantage with fluticasone furoate over generic fluticasone propionate.

Table 4. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Treatment of Allergic Rhinitis (perennial and seasonal)				
Chervinsky et al[44] Ciclesonide 200 µg DAILY vs placebo	DB, MC, PC, PG, RCT Patients 12 years or older with a 2 year history of PAR, who require continuous treatment and demonstrated skin prick test sensitivity to at least one allergen known to induce PAR	N=663 52 weeks	Primary: Treatment-emergent adverse events, 24 hour urinary free cortisol and morning cortisol levels at weeks 24 and 48 Secondary: Change from baseline in patient evaluated morning 24 hour rTNSS, PANS score at the end of treatment, combined RQLQ scores at end point	Primary: There was no clinically significant differences in the incidence of treatment-emergent adverse events; ciclesonide 75.1% vs placebo 74.3% (*P* value not reported). No clinically significant differences were seen between the ciclesonide and placebo groups with regards to 24 hour urinary free cortisol and morning cortisol levels and ocular examinations. Secondary: There was a significantly greater reduction from baseline in 24 hour rTNSSs in the ciclesonide group (-2.3) compared to placebo (-1.8) (*P*<0.001). No appreciable differences were found between ciclesonide and placebo groups in PANS score at the end of treatment. At the end point, ciclesonide produced a greater improvement in combined RQLQ scores compared to placebo (-1.07 vs -0.88; *P*=0.04).
Meltzer et al[47] Ciclesonide 200 µg DAILY vs placebo	DB, MC, PC, RCT Patients 12 years old or older with a 2 year history of PAR, who required continuous or intermittent treatment and demonstrated skin prick test sensitivity to at least one allergen known to induce PAR	N=676 6 weeks	Primary: Change from baseline in the average of morning and evening rTNSS Secondary: Average morning and evening patient evaluated instantaneous TNSSs, PANS score at the end of treatment, combined RQLQ	Primary: Ciclesonide 200 µg DAILY significantly reduced average morning and evening rTNSS compared to placebo; -2.51 vs -1.89 (*P*<0.001). Secondary: Ciclesonide 200 µg DAILY significantly reduced average morning and evening iTNSS through 6 weeks of therapy (*P*=0.001). A greater decrease from baseline was observed at the end of treatment in PANS scores for the ciclesonide group compared to the placebo group (*P*=0.051). There was a significant improvement seen in the ciclesonide group compared to placebo in combined RQLQ scores at the end of treatment; -1.30 vs -1.01 (*P*=0.01).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			score at the end of treatment	
Ratner et al[48] Ciclesonide 200 µg DAILY vs placebo	DB, MC, PC, PG, RCT Patients 12 years or older with a 2 year history of SAR who require treatment and demonstrated skin prick test sensitivity to mountain cedar pollen	N=327 4 weeks	Primary: Change from baseline in average morning and evening rTNSSs Secondary: Patient assessed iTNSSs, PANS score at days 15 and 29, total nasal symptom scores, combined RQLQ scores at days 15 and 29, individual nasal symptoms, time to onset of effect, adverse events	Primary: Over 2 weeks, ciclesonide 200 µg DAILY significantly improved the average morning and evening rTNSS compared to placebo; -2.40 vs -1.50 (P<0.001). The change from baseline over the entire study period was significant for the ciclesonide group compared to placebo (P<0.001). Secondary: By 2 weeks, ciclesonide 200 µg DAILY improved iTNSS compared to placebo (P<0.001). At day 15, treatment with ciclesonide provided significantly greater improvements in overall PANS and combined RQLQ scores compared to placebo (P≤0.002). By the end of the study statistically significant differences were not seen between the ciclesonide and placebo groups (P value not reported). The ciclesonide group had a greater response in reflective nonnasal symptoms scores compared to placebo however this was not statistically significant (-1.73 vs -1.30; P=0.071). By day 15, treatment differences for nasal symptoms favoring ciclesonide were evident (P<0.001). Significant improvements in average morning and evening rTNSSs with ciclesonide over placebo were seen by the second day of treatment (P<0.05). Frequency of adverse events were similar between treatment groups; ciclesonide 40.2% vs placebo 39.3%. The most common side effects for the ciclesonide group included nasal passage irritation (6.1%) and headache (5.5%).
Ratner et al[49] Ciclesonide 25 µg	DB, MC, PC, PG, Phase II, RCT	N=726 14 days	Primary: Change from baseline in sum of	Primary: Ciclesonide 100 µg/day and 200 µg/day, significantly improved the sum of morning and evening rTNSS compared to placebo. (P=0.04 and P=0.003).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
DAILY vs ciclesonide 50 µg DAILY vs ciclesonide 100 µg DAILY vs ciclesonide 200 µg DAILY vs placebo	Adult patients aged 18 to 65 years old with a 2 year history of SAR, experiencing nasal allergy symptoms, with a minimum score of 8 in either morning or evening rTNSS for at least 3 days during baseline period		morning and evening rTNSS Secondary: Change from baseline in the sum of morning and evening iTNSS, use of rescue medications	The average change from baseline in rTNSS was -4.2 for placebo and -4.8, -4.8, -5.3, and -5.8 for ciclesonide 25, 50, 100 and 200 µg/day, respectively. Secondary: Both ciclesonide 100 and 200 µg/day demonstrated greater improvements in iTNSS compared to placebo (*P* value not reported). There were no appreciable differences in the use of rescue medication, chlorpheniramine maleate, across all treatment groups.
Fokkens et al[45] Fluticasone furoate 110 µg DAILY vs placebo	DB, MC, PC, PG, RCT Patients ≥12 years old with SAR (defined as onset and offset of nasal allergy symptoms during each of the past two grass pollen seasons), and either a positive skin prick test to grass pollen or a positive in vitro test for specific IgE, within 12 months prior to the study	N=285 2 weeks	Primary: Mean change from baseline over the entire treatment period in daily rTNSS Secondary: Mean change from baseline over the entire treatment period in daily rTOSS, morning predose iTNSS, overall evaluation of response to therapy, mean change from baseline in RQLQ, iTOSS, daily	Primary: The mean change from baseline in daily rTNSS over the treatment period was greater for fluticasone furoate as compared to placebo (-4.94 and -3.18, respectively; LS mean difference, -1.757; *P*<0.001). Secondary: Fluticasone furoate was significantly more effective than placebo in improving daily rTOSS (-3.00 and -2.26, respectively; LS mean difference, -0.741; *P*<0.001) as well as in improving morning predose iTNSS (-4.50 and -2.60, respectively; LS mean difference -1.898; *P*<0.001). In terms of overall response to therapy, 67% of patients receiving fluticasone furoate reported significant or moderate improvement, compared to 39% of patients given placebo (*P*<0.001). Overall RQLQ core was decreased by 2.23 points in the fluticasone furoate group and by 1.53 points in the placebo group (difference of -0.7; *P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			reflective and instantaneous individual symptom scores, time to onset of action	
Gradman et al[50] Fluticasone furoate 110 µg DAILY vs placebo	DB, NI, PC, RCT, XO Prepubertal children (6-11 years of age) with a diagnosis of PAR or SAR for at least one year, and either a positive skin prick test or a positive test for the specific IgE to an appropriate seasonal or perennial allergen	N=58 2 weeks	Primary: Mean growth rate in lower-leg length Secondary: Adverse events	Primary: A prespecified cutoff of no more than –0.20 mm/week was determined to be "noninferior". The treatment difference in adjusted mean lower-leg growth rate between fluticasone furoate and placebo was –0.016 mm/week (95% CI, –0.13 to 0.10) demonstrating noninferiority. Secondary: Reported adverse events were similar between the 2 groups.
Kaiser et al[46] Fluticasone furoate 110 µg DAILY vs placebo	DB, PC, PG, RCT Patients ≥12 years old with SAR caused by ragweed pollen, with seasonal allergy symptoms during each of the past 2 fall allergy seasons; positive skin prick test response to ragweed allergen within 12 months	N=299 2 weeks	Primary: Mean change from baseline over the entire treatment period in daily rTNSS Secondary: Mean change from baseline over the entire treatment period in daily rTOSS, morning predose iTNSS, overall evaluation of response to therapy,	Primary: Fluticasone furoate significantly reduced nasal symptoms vs placebo, with a treatment difference of -1.473 (P<0.001). Secondary: An observed difference of -0.600 (P=0.004) between groups was recorded for the mean change from baseline in daily rTOSS over the entire treatment period. Fluticasone furoate demonstrated a significant reduction in morning predose iTNSS of -1.375 compared with placebo (P<0.001). A total of 73% of patients receiving fluticasone furoate vs 52% of placebo-treated patients reported improvement in their overall evaluation of response to therapy (P<0.01); significant moderate improvement was

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	prior to start of study; only moderate-to-severe nasal and ocular symptoms; during 2005 fall ragweed allergy season		HRQL based on RQLQ	noted in 42% of fluticasone-treated patients and 21% of placebo-treated patients. Fluticasone furoate-treated patients reported significant improvements in the overall RQLQ score vs those in the placebo group (-0.606; *P*<0.001). Adverse events occurred in 21% of patients receiving fluticasone furoate and 12% of patients that received placebo. The most common side effect was headache (>3%), which was seen more often with fluticasone furoate than placebo; epistaxis was another commonly reported side effect.
Maspero et al[51] Fluticasone furoate 100 µg DAILY vs fluticasone furoate 55 µg DAILY vs placebo	DB, MC, PC, PG, RCT Pediatric patients 2 to 11 years old with a ≥6 month history PAR documented by a positive skin prick test against an appropriate perennial allergen	N=558 12 weeks	Primary: Mean change from baseline in daily rTNSS over 4 weeks Secondary: Mean change from baseline in daily iTNSS, overall response to therapy, safety	Primary: Improvements in daily rTNSS over 4 weeks were not statistically significant compared to placebo for the fluticasone furoate 110 µg group; -0.452 (*P*=0.073). Patients treated with fluticasone furoate 55 µg had statistically significant improvements in daily rTNSS compared to placebo; -0.754 (*P*=0.003). Secondary: Both fluticasone furoate 55 µg (-0.751) and 110 µg (-0.651) showed significant improvements from baseline in daily iTNSS compared to placebo (*P*=0.002, *P*=0.009). Treatment differences, determined by overall response to therapy, were not significant for patients in the fluticasone furoate 110 µg group compared to placebo (*P*=0.414) but were significant for the fluticasone furoate 55 µg group (*P*=0.024). Treatment with both doses of fluticasone furoate was well tolerated over the 12 week period. Nasal examinations of were similar across all three treatment groups and ophthalmic examinations revealed no differences between groups in terms of mean change from baseline intraocular pressure in each eye. Treatment differences for mean change from baseline in 24 hour urinary cortisol excretion from placebo at either dose of fluticasone furoate were not statistically significant (*P* value not reported).
Martin et al[52]	DB, PC, PG, RCT	N=642	Primary:	Primary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Fluticasone furoate 55 µg DAILY vs fluticasone furoate 110 µg DAILY vs fluticasone furoate 220 µg DAILY vs fluticasone furoate 440 µg DAILY vs placebo	Patients 12 years or older with a diagnosis of SAR during the past two mountain cedar allergy seasons and a positive skin test to mountain cedar allergy	14 days	Mean change from baseline in daily rTNSS Secondary: Mean change from baseline in morning predose iTNSS, mean change from baseline in daily rTOSS and iTOSS, mean change from baseline in morning and evening rTNSS and iTNSS, overall response to therapy	Fluticasone furoate 55, 110, 220, and 440 µg DAILY demonstrated statistically significant improvements with respect to the mean change from baseline in daily rTNSS compared to placebo (P<0.001 for all measures). Secondary: Fluticasone furoate was significantly more effective than placebo for mean changes from baseline in morning predose iTNSS (P<0.001 each dose vs placebo), daily rTOSS (P≤0.013 each dose vs placebo), and iTOSS (P≤0.019 for fluticasone furoate 110, 220, and 440 µg/day vs placebo). Over the entire treatment period, all doses of fluticasone furoate demonstrated significantly greater efficacy compared to placebo with regards to morning and evening rTNSS and iTNSS scores (P<0.001 for all measures). At the end of the treatment period, patients treated with fluticasone furoate rated their overall response to therapy significantly better than those treated with placebo (P<0.001).
Rosenblut et al[53] Fluticasone furoate 110 µg DAILY vs placebo	DB, MC, PC, PG, RCT Patients >12 years old with a >2-year medical history and past treatment of PAR and a positive skin-prick test to an appropriate allergen either within the last 12 months prior to or at screening	N= 806 12 months	Primary: Safety and tolerability based on adverse event data graded by severity (mild, moderate, or severe) as well as through the use of 24-hour urine samples, ECG, other laboratory measures, and eye examinations Secondary: Not reported	Primary: Adverse events occurred in 77% of fluticasone furoate-treated patients and 71% of patients receiving placebo, where most were mild to moderate in intensity. The most frequently reported adverse events were headache and nasopharyngitis. Epistaxis was more frequently reported with patients given fluticasone furoate. There was no evidence of clinically relevant systemic corticosteroid exposure or impairment of HPA-axis function. Fluticasone furoate-treated patients had similar 24-hour urine cortisol results to those receiving placebo. There were no clinically meaningful differences between the groups in terms of other safety assessments, including mean changes in ophthalmic parameters.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Secondary: Not reported
Vasar et al[54] Fluticasone furoate 110 µg DAILY vs placebo	DB, PC, PG, RCT Patients 12 years or older with a history of PAR for ≥2 years and a positive skin-prick test to an appropriate perennial allergen	N=302 6 weeks	Primary: Mean change from baseline in rTNSS Secondary: Mean change from baseline in morning predose iTNSS, daily rTNSS, daily PNIF, and RQLQ scores, overall response to therapy, safety	Primary: The mean change from baseline in rTNSS was significantly greater in the fluticasone furoate 110 µg group (-3.95) compared to placebo (-2.69; *P*<0.001). Secondary: The mean change from baseline in morning predose iTNSS was significantly greater in fluticasone furoate patients (-3.82) compared to placebo (-2.36; *P*<0.001). Treatment with fluticasone furoate demonstrated significantly greater efficacy compared to placebo in terms of improvements in daily iTNSS (*P*=0.004), PNIF (*P*=0.004) and overall RQLQ scores (*P*<0.001). Thirty seven percent of patients treated with fluticasone furoate rated their overall response to therapy as "significantly improved" compared to 14% of patients treated with placebo (*P*<0.001). Treatment was well tolerated over the 6 week period.
Khanna et al[39] Beclomethasone, dose not specified vs budesonide, dose not specified vs fluticasone propionate, does not specified	SB, XO Patients with allergic rhinitis	N=114 Duration not specified	Primary: Sensory perceptions and patient reference Secondary: Not reported	Primary: Significantly more patients preferred mometasone because of less irritation, odor, and aftertaste (*P* values not reported). Fluticasone propionate was reported by patients as having a significantly higher odor strength and amount of irritation (*P* values not reported). Eighty percent of the patients predicted better compliance with their preferred drug. Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs mometasone, dose not specified				
Svendsen et al[13] Beclomethasone, dose not specified vs flunisolide, dose not specified	DB, RCT, XO Patients with perennial rhinitis	N=23 8 weeks	Primary: Rhinitis symptoms and patient preference Secondary: Not reported	Primary: There were no statistically significant differences in rhinitis symptoms or patient preference between treatments (*P* value not reported). Secondary: Not reported
Welsh et al[14] Beclomethasone 336 µg daily, administered as 2 sprays in each nostril BID vs flunisolide 200 µg daily, administered as 2 sprays in each nostril BID vs cromolyn 41.6 mg daily, administered as 1 spray in each nostril QID vs	PC, RCT Patients 12-50 years of age, with at least 2 year history of SAR and positive skin test to crude short ragweed extract	N=120 8 weeks	Primary: Symptomatic relief Secondary: Adverse events	Primary: Beclomethasone, flunisolide, and cromolyn significantly reduced the use of supplemental antihistamines or decongestants and hay fever symptoms such as sneezing, nasal symptoms, eye symptoms, itchy nose, and throat symptoms compared with placebo (*P*<0.001). Beclomethasone and flunisolide significantly reduced hay fever symptoms compared to cromolyn (*P*<0.001). There were no statistically significant differences between beclomethasone and flunisolide in relief of hay fever symptoms (*P* value not reported). Secondary: There was significantly more nasal burning with flunisolide than the other treatments (*P*<0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
placebo				
Al-Mohaimeid[15] Budesonide 200 µg BID vs beclomethasone 200 µg BID	RCT, SB Patients 18-70 years of age, with perennial allergic rhinitis	N=120 3 weeks	Primary: Nasal symptoms Secondary: Not reported	Primary: There were statistically significant fewer reports of sneezing with budesonide than beclomethasone (*P*=0.04). No statistically significant differences in the other symptoms, such as blocked nose, runny nose, itchy nose, runny eyes, and sore eyes, were reported (*P*>0.05). After 3 weeks of treatment, more patients reported being totally free of symptoms with budesonide than with beclomethasone (38% vs 27%; no *P* value reported). More patients reported the treatment as noticeably, very, or totally effective with budesonide than with beclomethasone (72% vs 58%; *P* value not reported).). Secondary: Not reported
McArthur[16] Budesonide 200 µg BID vs beclomethasone 200 µg BID	DB, RCT Adults with SAR	N=88 3 weeks	Primary: Nasal and non-nasal symptom score Secondary: Adverse events	Primary: Budesonide treatment resulted in significantly lower scores for runny nose, itchy nose, and sneezing compared with beclomethasone at all time points (*P*<0.05), but the greatest difference was towards the end of the treatment period. There was no statistically significant difference between treatment groups in scores for nasal blockage, runny eyes, and sore eyes (*P* value not reported). Secondary: Adverse events for both treatments were mild and transient.
Vanzieleghem et al[17] Budesonide as needed,	DB, DD, RCT Patients with SAR	N=61 7 weeks	Primary: Nasal symptoms, use of chlorpheniramine	Primary: Less budesonide was administered by the subjects than beclomethasone to maintain good control of nasal symptoms (*P*=0.016).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
up to 2 sprays of 50 µg/spray in each nostril QID vs beclomethasone as needed, up to 2 sprays of 50 µg/spray in each nostril QID	during the ragweed-pollen season		as rescue medication Secondary: Adverse events	No statistically significant difference was observed between treatment groups in the amount of oral chlorpheniramine used as rescue medication (*P*=NS). Secondary: Reported adverse events with both treatments were mild and transient.
Andersson et al[18] Budesonide 200 or 400 µg DAILY vs fluticasone propionate 200 µg DAILY vs placebo	MC, PC, PG, RCT Patients with PAR	N=98 6 weeks	Primary: Rhinitis symptoms, use of terfenadine as rescue medication Secondary: Safety as assessed by rhinoscopy, urine cortisol, adverse events	Primary: There were no significant differences in nasal symptoms or eye symptoms between active treatment groups (*P* value not reported). All active treatments reduced the use of terfenadine when compared with baseline, but this was significantly significant with budesonide only (*P*<0.05). Secondary: Reported adverse events were few and minor. No significant differences in adverse events or 24-hour cortisol levels were reported between treatment groups (*P* value not reported).
Day et al[19] Budesonide 256 µg DAILY vs fluticasone propionate 200 µg DAILY	DB, MC, PC, PG, RCT Patients ≥18 years of age with at least a 1-year history of PAR and positive skin test to one or more perennial allergens	N=273 6 weeks	Primary: Nasal symptoms, patients' overall evaluation of efficacy, and use of rescue medication Secondary: Adverse events	Primary: Both treatments resulted in significantly greater improvement in combined nasal symptom scores, runny nose, and sneezing from baseline compared with placebo (*P*≤0.0012). Budesonide showed greater improvement in combined nasal symptom scores (*P*=0.031) and nasal blockage (*P* value not reported) than fluticasone propionate, but no statistically significant differences in runny nose or sneezing symptoms were detected (*P* value not reported). Significant improvements in nasal symptoms were seen at 36 hours with budesonide and 60 hours with fluticasone propionate (*P* value not reported). At 6 weeks of treatment, there were no statistically significant differences

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				in patients' overall evaluation of efficacy (*P*=0.44) or use of antihistamines as rescue medication (no *P* values reported) between treatment groups. Secondary: The rates of reported adverse events were 46% with budesonide, 37% with fluticasone propionate, and 36% with placebo (no *P* values reported). No signs of fungal infection were detected in the study population.
Shah et al[40] Study 1: Budesonide 32 µg in each nostril for one dose vs fluticasone propionate 100 µg in each nostril for one dose Study 2: budesonide 32 µg in each nostril for one dose vs fluticasone propionate 50 µg in each nostril for one dose	MC, RCT, SB, XO Patients ≥18 years of age, with ≥1 year history of allergic rhinitis and experiencing mild to moderate symptoms	N=181 (Study 1) N=190 (Study 2) 1 day	Primary: Sensory Perceptions Questionnaire and patients' product preference Secondary: Adverse events	Primary: In study 1, significantly fewer patients perceived the scent (*P*<0.001), taste (*P*<0.001), aftertaste (*P*<0.001), throat rundown (*P*<0.001), and nose run out (*P*<0.019) with budesonide than with fluticasone propionate. In study 2, significantly fewer patients detected an altered scent or taste with budesonide than with fluticasone propionate (*P*<0.001). There were no significant differences between budesonide and fluticasone propionate in aftertaste, throat rundown, and nose run out. More patients perceived the spray in the throat as less wet (*P*<0.004 for study 1 and *P*<0.002 for study 2) and therefore preferred the feel of the spray in the throat (*P*<0.001 for both studies) of budesonide to that of fluticasone propionate. More patients perceived the spray in the nose as less wet (*P*<0.001 for both studies) and therefore preferred the feel of the spray in the nose (*P*<0.001 for both studies) of budesonide to fluticasone propionate. Significantly more patients perceived a less forceful spray with budesonide and therefore preferred budesonide to fluticasone propionate (*P*<0.001). Overall, significantly more patients preferred budesonide to fluticasone propionate (*P*=0.02). Secondary: Budesonide and fluticasone propionate were both well tolerated.
Stern et al[20]	MC, PC, PG, RCT	N=635	Primary: Nasal and eye	Primary: Budesonide and fluticasone propionate resulted in significant

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Budesonide 128 µg or 256 µg DAILY vs fluticasone propionate 200 µg DAILY vs placebo	Patients 18-72 years of age, with at least a 2-year history of allergic rhinitis	4-6 weeks	symptoms Secondary: Adverse events	improvements in individual nasal symptoms such as blocked nose, runny nose, and sneezing (P<0.001), combined nasal symptoms (P<0.001), eye symptoms (P value not reported), and overall substantial or total control of symptoms (P<0.001) compared to placebo. Budesonide 256 µg produced significant reduction in sneezing compared with fluticasone propionate (P=0.04). There were no other significant differences in individual nasal symptoms, combined nasal symptoms, eye symptoms, or overall substantial or total control of symptoms between treatment groups (P values not reported). Secondary: Budesonide and fluticasone propionate were well tolerated, with reported adverse events mild to moderate in severity.
Naclerio et al[21] Budesonide 32 µg in each nostril DAILY vs mometasone 100 µg in each nostril DAILY	PG, RCT Patients >18 years of age with PAR, who were symptomatic on the majority of days of each year and had a positive skin test to dust mites	N=20 2 weeks	Primary: Symptomatic relief and quality of life as assessed by the RQLQ and nasal clearance Secondary: Not reported	Primary: The RQLQ scores showed that both budesonide and mometasone resulted in a significant improvement in quality of life compared with baseline (P value not reported). There were no significant differences between treatment groups for any of the individual domains in the RQLQ (P value not reported). Data on nasal clearance could not be interpreted by the authors. Secondary: Not reported
Aasand et al[22] Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	MC, PG, SB Patients with at least a 2-year history of seasonal rhinitis	N=47 4 weeks	Primary: Nasal symptoms Secondary: Adverse events	Primary: Flunisolide and beclomethasone improved nasal rhinitis symptoms (88% of patients showed improvement with flunisolide vs 91% with beclomethasone; P value not reported). No statistical differences were observed between treatment groups (P value not reported). Secondary: The only reported adverse event with both medications was mild stinging of transient duration.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Langrick[23] Flunisolide 200 µg daily, administered as 2 sprays in each nostril BID vs beclomethasone 400 µg daily, administered as 2 sprays in each nostril BID	PG, RCT, SB Patients 18-60 years of age, with a history of moderate to severe hay fever	N=69 7 weeks	Primary: Signs and symptoms of hay fever, severity of symptoms, and physicians' and patients' evaluation of overall effect of treatment Secondary: Adverse events	Primary: There were no significant differences between treatment groups in severity of symptoms, overall treatment effect, or patients' self-assessment of symptoms such as sneezing, runny nose, and blocked nose (*P* value not reported). Secondary: One patient in the flunisolide reported a dry throat of moderate severity. One patient in the beclomethasone group reported a mild tickling sensation inside the nose.
McAllen et al[24] Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	SB, XO Patients 19-58 years of age who had perennial rhinitis with or without seasonal exacerbations and had moderate to severe symptoms of 6 months to 50 years in duration	N=34 8 weeks	Primary: Rhinitis symptoms Secondary: Adverse events and *Candida* growth	Primary: Treatment with flunisolide and beclomethasone significantly reduced sneezing, stuffiness, runny nose, nose-blowing, and interference with routine life when compared with baseline (*P* value not reported). There were no statistical differences between the flunisolide and beclomethasone treatment groups in nasal symptoms, physicians' and patients' preference, and interference with routine life (*P* value not reported). Secondary: Neither treatment resulted in *Candida* growth. Reported side effects were minor and were mostly nasal irritation or dryness.
Sahay et al[25] Flunisolide 50 µg in each nostril BID vs	OL, PG Patients with perennial allergic rhinitis, with or without SAR	N=56 4 weeks	Primary: Symptom relief Secondary: Detection of *Candida* growths and safety	Primary: Flunisolide and beclomethasone resulted in significant reductions in sneezing, stuffiness, runny nose, nose blowing, postnasal drip, epistaxis, and interference by symptoms with routine life or sleep when compared to baseline (*P*<0.01 for all).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
beclomethasone 50 µg in each nostril QID				There were no statistically significant differences in control of symptoms between the two treatment groups (*P* value not reported). Secondary: There were no signs of adrenal suppression or *Candida* growths in either group. There were four side effects in the flunisolide group and five side effects in the beclomethasone group that were considered to be probably drug related (*P* value not reported).
Sipila et al[26] Flunisolide 50 µg in each nostril BID vs beclomethasone 50 µg in each nostril QID	comparative, OL, PG Patients with allergic rhinitis and seasonal symptoms for at least two years	N=45 4 weeks	Primary: Daily symptoms and severity of nasal symptoms Secondary: Adverse events	Primary: There were no significant differences between the treatment groups in the change from baseline in daily symptoms such as runny nose, stuffiness, sneezing, and eye symptoms (*P* value not reported). Improvement in the severity of nasal symptoms compared with baseline was similar in both treatment groups (*P* value not reported). Secondary: The reported side effects were mild and primarily consisted of local irritation.
Haye et al[27] Fluticasone propionate 200 µg BID vs beclomethasone 200 µg BID	DB, MC, PG, RCT Patients ≥16 years of age with perennial rhinitis	N=251 1 year	Primary: Rhinitis symptoms Secondary: Safety	Primary: Fluticasone propionate treatment resulted in significantly less nasal blockage (*P*=0.002), nasal discharge (*P*=0.002), and eye watering/irritation (*P*=0.048) than beclomethasone. No significant differences were observed in the amount of sneezing (*P*=0.114) or nasal itching (*P*=0.052) between treatment groups. Secondary: There were no significant differences in nasal itching (*P*=0.052), sneezing (*P* value not reported), nasal examination by rhinoscopy, hematologic, biochemical, and urinary parameters, plasma cortisol level, or adverse events (*P* values not reported) between treatment groups.
LaForce et al[28]	DB, MC, PC, PG, RCT	N=238	Primary: Nasal symptoms	Primary: Fluticasone propionate reduced patient-rated nasal symptom scores

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Fluticasone propionate 100 µg BID or 200 µg DAILY vs beclomethasone 168 µg BID vs placebo	Patients at least 12 years of age, with at least a 2-year history of SAR, who have positive skin test to at least one spring allergen and moderate to severe symptoms	4 weeks	Secondary: Adverse events	significantly better than beclomethasone (P<0.05) and placebo (P<0.01) at all time points measured. There were no statistically significant differences in clinician-rated nasal symptom scores between treatment groups (P=NS). Secondary: There were no significant differences in adverse events between treatment groups (P value not reported).
Ratner et al[29] Fluticasone propionate 200 µg DAILY vs beclomethasone 168 µg BID vs placebo	DB, MC, PC, PG, RCT Adult patients with at least a 2-year history of SAR, who have moderate to severe symptoms and positive skin test to mountain cedar	N=313 2 weeks	Primary: Nasal symptoms, overall response to treatment, and use of rescue medication (chlorpheniramine maleate) Secondary: Adverse events	Primary: When compared with placebo, significant improvements in nasal symptoms and overall response to treatment were seen with fluticasone propionate and beclomethasone as evaluated by the clinicians and the patients (P<0.05 for all). There were no statistically significant differences between treatment groups in nasal symptoms as rated by the clinicians or the patients or overall response to treatment (P value not reported). When compared with placebo, there was a significant reduction in the use of rescue medication with fluticasone propionate and beclomethasone (P<0.05). There was no statistically significant difference between treatment groups in the amount of rescue medication used (P value not reported). Secondary: No clinically significant differences in any of the safety variables between treatment groups were reported.
Van As et al[30] Fluticasone propionate 100 µg BID or 200 µg DAILY	DB, MC, PC, PG, RCT Patients 12-71 years of age, with PAR and moderate	N=466 6 months	Primary: Nasal symptoms and use of antihistamine as rescue medication Secondary:	Primary: Fluticasone and beclomethasone reduced nasal obstruction, rhinorrhea, sneezing, nasal itching, and nasal eosinophilia (P value not reported). There were no significant differences between active treatment groups in nasal symptoms, number of patients who used rescue medication, amount

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs beclomethasone 168 µg BID vs placebo	to severe symptoms, nasal eosinophils, and positive skin test to a perennial allergen		Adverse events	of rescue medication consumed, or incidences of adverse events (*P* value not reported). Secondary: No evidence of systemic effects with drug treatment was reported.
Bachert et al[55] Fluticasone propionate 200 µg DAILY vs triamcinolone 220 µg DAILY vs placebo	DB, PC, RCT, XO Healthy volunteers 18-65 years of age	N=23 12 days	Primary: Suppression of the HPA axis as measured by 12 hour overnight urinary cortisol excretion and serum cortisol concentrations Secondary: Adverse events	Primary: Overnight urinary cortisol concentrations showed that there was no significant difference in HPA axis suppression with fluticasone propionate (*P*=0.609) or triamcinolone (*P*=0.194) compared with placebo. Neither fluticasone propionate (*P*=0.999) and triamcinolone (*P*=0.521) showed a significant effect on the HPA axis activity when compared with placebo, as assessed by the mean peak serum cortisol concentrations before and after ACTH stimulation. Secondary: Both medications were well tolerated. There were no significant differences in the number of subjects that experienced adverse events between treatment groups (1 with fluticasone propionate, 2 with triamcinolone, 3 with placebo; *P* value not reported).
Drouin et al[31] Mometasone 100 µg in each nostril DAILY vs beclomethasone 100 µg in each nostril BID vs placebo	DB, DD, MC, PC, PG, RCT Patients 12 years of age and older, who are allergic to at least one perennial allergen, with adequate symptomatology	N=427 12 weeks	Primary: Change from baseline in total morning plus evening diary nasal symptom score over the first 15 days of treatment Secondary: Total diary nasal symptom scores averaged over 15-day intervals beyond	Primary: When compared to placebo, both mometasone and beclomethasone produced significantly greater improvements in the total morning plus evening diary nasal symptom scores over the first 15 days of treatment (*P*≤0.01). The difference in reduction from baseline in nasal symptom scores between mometasone and beclomethasone was not significant at any time point (*P*≥0.32). Secondary: Physician evaluations of nasal symptoms for mometasone and beclomethasone were not statistically different from each other at any time

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			day 15, composite total and individual diary symptom scores, physician evaluation of response to therapy, and adverse events	point (*P* value not reported). The rates of adverse events were similar for all groups (43% for mometasone, 42% for beclomethasone, 36% for placebo; *P* value not reported).
Graft et al[56] Mometasone 100 µg in each nostril DAILY vs beclomethasone 84 µg in each nostril BID vs placebo	DB, MC, PC, PG, RCT Patients at least 12 years of age who have at least a 2-year history of moderate to severe SAR and a positive skin test response to ragweed	N=349 8 weeks	Primary: Severity score of nasal and non-nasal symptoms Secondary: Adverse events	Primary: Both treatments resulted in a significantly higher percentage of days with minimal symptoms, longer duration to the first occurrence of a non-minimal symptom day, and total nasal symptom scores compared with placebo (*P*≤0.01 for all). There was no statistically significant difference in the percentage of days with minimal symptoms between treatment groups (*P* value not reported). Nasal symptom scores for the treatment period before the allergy season onset were significantly lower with mometasone than beclomethasone (*P*=0.05). Secondary: The percentages of patients experiencing at least one adverse event that was considered possibly related to treatment are as follows: 16% of the mometasone group, 14% of the beclomethasone group, and 19% of the placebo group (*P* value not reported). The adverse events were generally mild to moderate and of short duration.
Hebert et al[32] Mometasone 100 or 200 µg DAILY, administered as 2 sprays of 25 or 50 µg/spray in each nostril DAILY vs	DB, DD, MC, PC, PG, RCT Patients 18 years of age and older, with moderate to severe SAR for at least 2 years, who have a positive skin test to at least one	N=501 4 weeks	Primary: Nasal symptom score, physicians' and patients' evaluation of response to therapy, and use of loratadine as rescue medication Secondary:	Primary: Nasal symptoms (*P*≤0.01) and use of rescue medication (*P*≤0.05) were significantly improved in all three treatment groups compared with placebo. There were no significant differences between treatment groups in nasal symptom score, physicians' evaluation of nasal symptoms, overall condition, and response to treatment, or use of rescue medication (*P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
beclomethasone 100 µg in each nostril BID vs placebo	tree and/or grass aeroallergen		Adverse events	Secondary: The rate of adverse events were similar in all groups (25% with mometasone 100 µg, 26% with mometasone 200 µg, 30% with beclomethasone, 28% with placebo; *P* value not reported).
Mandl et al[33] Mometasone 100 µg in each nostril DAILY vs fluticasone propionate 100 µg in each nostril DAILY vs placebo	DB, DD, PC, PG, RCT Patients 12-77 years of age, who are allergic to at least one perennial allergen, and have moderate to severe symptomatology	N=550 12 weeks	Primary: Nasal symptom score Secondary: Physicians' evaluation of nasal symptoms and response to therapy and adverse events	Primary: Both mometasone and fluticasone propionate produced significantly greater improvements in nasal symptoms than placebo ($P<0.01$). The difference in reduction of nasal symptom score between mometasone and fluticasone propionate was not significant at any time point ($P\geq0.43$). Secondary: Physicians' evaluation of nasal symptoms and response to therapy were similar for mometasone and fluticasone propionate (*P* value not reported). The rates of adverse events were similar for all groups (33% for mometasone, 38% for fluticasone propionate, 37% for placebo; *P* value not reported).
Meltzer et al[41] Mometasone, dose not specified vs fluticasone propionate 200 µg	DB, RCT, XO Patients with allergic rhinitis	N=100 Duration not specified	Primary: Individual product sensory attributes and overall sensory preference Secondary: Not reported	Primary: Significantly more patients preferred mometasone to fluticasone propionate for its scent ($P=0.0005$), immediate taste ($P=0.005$), aftertaste ($P=0.005$), and overall (54% vs 33%; $P=0.03$). Patients rated mometasone as significantly better than fluticasone propionate in individual sensory attributes, which included fewer perceived scent/odor ($P<0.001$), taste ($P=0.002$), and aftertaste ($P=0.007$). Patients reported significantly larger percentage of expected compliance with mometasone than fluticasone propionate (47% vs 25%; $P=0.03$). Secondary: Not reported
Lumry et al[34]	MC, PG, RCT, SB	N=152	Primary: Nasal symptoms, eye	Primary: Significant improvement from baseline in rhinitis related-nasal and eye

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Triamcinolone 220 µg DAILY vs beclomethasone 168 µg BID	Patients at least 18 years of age with at least a 2-year history of SAR to ragweed pollen	3 weeks	symptoms, HRQL, and patient preference for sensory attributes Secondary: Adverse events	symptoms were seen with triamcinolone and beclomethasone (*P* value not reported). There were no significant differences in nasal stuffiness, nasal discharge, nasal index, nasal itching, total eye symptoms, patients' or physicians' overall assessment of efficacy, or HRQL between treatment groups (*P* value not reported). Patients rated the taste and odor of triamcinolone as significantly better than beclomethasone ($P \leq 0.05$). Otherwise, there were no statistically significant differences between treatment groups in the other sensory attributes such as medication running down to throat, medication running out of nose, medication induced sneezing, stinging/burning sensation, nose bleed, and blood in mucus ($P > 0.05$). Secondary: The rates of reported adverse events were comparable between treatment groups (34.7% with triamcinolone vs 35.1% with beclomethasone; *P* value not reported).
Winder et al[35] Triamcinolone 220 µg DAILY vs beclomethasone 84 µg BID	MC, PG, RCT, SB Patients 18-64 years of age, with at least a 2-year history of PAR who have positive skin tests to indoor allergens and nasal eosinophilia or basophilia	N=169 4 weeks	Primary: Rhinitis symptoms and global evaluations of treatment by patients and physicians Secondary: Adverse events	Primary: No statistically significant differences were found in rhinorrhea, congestion, sneezing, sum of primary symptom scores, and physicians' global evaluations between treatment groups (*P* value not reported). Patients' global evaluation of treatment with triamcinolone were significantly higher than with beclomethasone ($P < 0.05$). Secondary: There were no statistically significant differences between treatments in burning/stinging, nasal dryness, nasal bleeding, bloody mucus, nasal congestion, throat discomfort, and bad taste (*P*=NS). There were significantly more medication-induced sneezing with triamcinolone than beclomethasone ($P = 0.024$). There was significantly more medication runoff from the nose and throat

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				with beclomethasone than triamcinolone (P<0.05).
Bachert et al[42] Triamcinolone 110 µg in each nostril DAILY vs fluticasone propionate 100 µg in each nostril DAILY vs mometasone 100 µg in each nostril DAILY	DB, MC, RCT, XO Patients at least 18 years of age, with at least a 2- year history of allergic rhinitis	N=95 1 day	Primary: Sensory perceptions, patient preferences, and likelihood of compliance Secondary: Not reported	Primary: Overall, more patients preferred triamcinolone to fluticasone propionate (P≤0.05) and mometasone (P≤0.001). Patients preferred the odor, sensation of greater moisture, less aftertaste, and less irritation of triamcinolone to that of fluticasone propionate and mometasone (P<0.05 for all). Triamcinolone was significantly preferred more than mometasone for the taste, comfort, and less irritation (P<0.05 for all). Fluticasone propionate was also significantly preferred more than mometasone in terms of taste, comfort and amount of irritation (P≤0.05). There were no significant differences between fluticasone propionate and mometasone in aftertaste and amount of irritation (P value not reported). Patients reported a higher likelihood of compliance with triamcinolone (67.4%) than with fluticasone propionate (54.7%) and mometasone (49.5%); P value not reported. Secondary: Not reported
Gross et a36 Triamcinolone 110 µg in each nostril DAILY vs fluticasone propionate 100 µg in each nostril DAILY	AC, PG, RCT, SB Patients 12-70 years of age, with fall SAR and positive skin test to ragweed	N=352 3 weeks	Primary: Nasal symptoms, effects on HRQL as measured by RQLQ, adverse events Secondary: Not reported	Primary: No statistically significant differences were reported between the treatment groups in daily total nasal symptom scores (P=0.332), individual symptom scores (P value not reported), treatment-related side effects (P value not reported), overall HRQL scores (P=0.4), or overall RQLQ scores (P value not reported). Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Small et al[37] Triamcinolone 110 µg in each nostril DAILY vs fluticasone propionate 100 µg in each nostril DAILY	MC, PG, RCT, SB Patients 12-70 years of age with spring pollen allergic rhinitis for at least 2 years, who had at least two nasal symptoms (rhinorrhea, congestion, sneezing, and itching) at baseline, and who had a Rhinitis Index Score of at least 24 out of 48	N=233 21 days	Primary: Rhinitis Index Score and individual symptom score Secondary: Physicians' and patients' global evaluations, patients' acceptance of the study medications, and safety	Primary: There were no significant differences between treatment groups in the changes from baseline in Rhinitis Index Score (*P*=0.23) or individual symptoms, such as congestion (*P*=0.58), rhinorrhea (*P*=0.08), sneezing (*P*=0.51), and nasal itching (*P*=0.64). Secondary: There were no statistically significant differences between treatment groups in physicians' and patients' global evaluations (*P* value not reported). Patients' acceptance of the study medication varied. Fluticasone propionate was rated as significantly more intolerable than triamcinolone with respect to medication "running down the throat" and "medication running out of nose" (*P*<0.01), while triamcinolone was rated as significantly more intolerable than fluticasone propionate with respect to "medication causing dry nostril" and "medication causing stuffed-up nose" (*P*<0.01). Adverse events were experienced by 26% of the patients receiving triamcinolone and 22% of the patients receiving fluticasone propionate (*P* value not reported).
Stokes et al[43] Triamcinolone 220 µg one time vs fluticasone propionate 200 µg one time vs mometasone 200 µg one time	DB, MC, RCT, XO Patients 18-70 years of age, with at least a 2-year history of allergic rhinitis, who were symptomatic at baseline	N=215 1 day	Primary: Patients' sensory perception measured by the NSEQ, patients' preference measured by the ONSEQ, patients' self reported expected compliance score using the 4-point Likert scale Secondary: Not reported	Primary: The NSEQ scores for triamcinolone were significantly higher than fluticasone propionate and mometasone (78.6 for triamcinolone, 72.3 for fluticasone propionate, 69.3 for mometasone; *P*<0.001 for all). Based on the ONSEQ scores, significantly more patients preferred triamcinolone (50% for triamcinolone vs 25% for fluticasone propionate and 25% mometasone; *P*<0.001 for all). A larger percentage of the patients reported a Likert score of 1 or "definitely complying" with triamcinolone (62.5% for triamcinolone, 49.0% for fluticasone, 51.0% for mometasone; *P*<0.01 for all). Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Not reported
Treatment of Nonallergic Rhinitis				
Scadding et al[38] Fluticasone propionate 200 µg DAILY or BID vs beclomethasone 200 µg BID vs placebo	DB, MC, PC, PG, RCT Patients with allergic and nonallergic perennial rhinitis	N=not specified 12 weeks	Primary: Nasal symptoms Secondary: Adverse events	Primary: There were no significant differences between active treatment groups in nasal symptoms (*P* value not reported). Secondary: Few adverse events and no treatment-related abnormalities in laboratory measurements were reported.

Drug regimen abbreviations: BID=twice daily, QID=four times daily
Study abbreviations: AC=active-controlled, DB=double-blind, DD=double-dummy, MC=multi-center, NI=noninferiority, NS=nonsignificant, OL=open-label, PC=placebo-controlled, PG=parallel-group, RCT=randomized controlled trial, SB=single-blinded, XO=cross-over
Miscellaneous abbreviations: ACTH=adrenocorticotropic hormone, ECG=electrocardiogram, HRQL=health related quality of life, HPA=hypothalamic-pituitary-adrenal, iTNSS=instantaneous total nasal symptom score, iTOSS=instantaneous total ocular symptom score, LS=least square, NSEQ=nasal spray evaluation questionnaire, ONSEQ=overall nasal spray evaluation questionnaire, PANS=physician assessed overall nasal signs and symptoms, PAR=perennial allergic rhinitis, PNIF=peak nasal inspiratory flow, RQLQ=rhinoconjunctivitis quality of life questionnaire, rTNSS=reflective total nasal symptom score, rTOSS=reflective total ocular nasal symptom score, SAR=seasonal allergic rhinitis

Special Populations

Table 5. Special Populations[4-11]

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Beclomethasone	No dosage adjustment necessary in the elderly. Approved for use in children ages 6 to 12 years old.	No renal dose adjustment required.	No hepatic dose adjustment required.	C	Unknown
Budesonide	Not studied in elderly. Approved for use in children ages 6 years and older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	B	Unknown
Ciclesonide	Not studied in elderly. Approved for use in children ages 6 years or older for seasonal allergic rhinitis. Approved for use in children ages 12 years or older for perennial allergic rhinitis	No renal dose adjustment required.	No hepatic dose adjustment required.	C	Unknown
Flunisolide	Not studied in the elderly Approved for use in children ages 6 years and older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown
Fluticasone furoate	No dosage adjustment necessary in the elderly. Approved for use in children ages 2 to 11 years old.	No renal dose adjustment required.	No hepatic dose adjustment required. Monitoring recommended in patients with severe hepatic dysfunction.	C	Unknown
Fluticasone propionate	No dosage adjustment necessary in the elderly. Approved for use in	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
	children ages 4 years and older.				
Mometasone	Not studied in elderly. Approved for use in children ages 2 years or older.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	C	Unknown
Triamcinolone	No dose adjustment required. Approved for use in children ages 2 to 12 years old.	No renal dose adjustment required.	No hepatic dose adjustment required.	C	Unknown

Adverse Drug Events

The most common adverse events reported with the use of intranasal corticosteroids include headache, pharyngitis, epistaxis, cough, nasal irritation and pharyngolarygneal pain. Reports of nasal septal perforation associated with the use of intranasal corticosteroids are rare.

Table 6. Adverse Drug Events [4-11]

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone furoate	Fluticasone propionate	Mometasone	Triamcinolone
Central Nervous System								
Dizziness	-	-	-	-	-	1-3	-	-
Headache	<5	-	6	-	8-9	7-16	17-26	≥2
Lightheadedness	<5	-	-	-	-	-	-	-
Gastrointestinal								
Abdominal pain	-	-	-	-	-	1-3	-	-
Diarrhea	-	-	-	-	-	1-3	2-<5	-
Dyspepsia	-	-	-	-	-	-	2-<5	-
Nausea	<5	-	-	>1	-	3-5	2-<5	-
Vomiting	-	-	-	-	-	3-5	1-5	≥2
Hypersensitivity reactions								
Anaphylaxis	-	-	-	-	-	Rare	✔	-
Angioedema	Rare	Rare	-	-	-	Rare	✔	-
Bronchospasm	Rare	-	-	-	-	Rare	-	-
Dyspnea	-	-	-	-	-	Rare	-	-
Edema of face/tongue	-	-	-	-	-	Rare	-	-
Pruritus	-	-	-	-	-	Rare	-	-
Rash	Rare	-	-	-	-	Rare	-	-
Wheezing	Rare	Rare	-	-	-	Rare	2-<5	-
Urticaria	Rare	-	-	-	-	Rare	-	-
Respiratory								
Asthma symptoms	-	-	-	-	-	3-7	2-<5	≥ 2
Bronchitis	-	-	-	-	-	1-3	2-<5	-
Bronchospasm	-	2	-	-	-	-	-	-
Cough	-	2	-	>1	3-4	4	7-13	2
Epistaxis	<3	8	5	3-9	4-6	6-7	8-11	3
Mild nasopharyngeal Irritation	24	-	3	-	2-4	-	-	-
Nasal burning/stinging	-	-	-	13	-	2-3	✔	-
Nasal dryness	✔	-	-	>1	-	-	-	-
Nasal irritation	✔	2	-	-	-	2-3	2-<5	-

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone furoate	Fluticasone propionate	Mometasone	Triamcinolone
Nasal mucosal ulceration	Rare	-	-	-	1	Rare	Rare	-
Nasal septal perforation	Rare	Rare	-	Rare	-	Rare	Rare	Rare
Nasal stuffiness/ congestion	<3	-	-	-	-	-	-	-
Rhinitis	-	-	-	-	-	-	2-<5	≥2
Pharyngitis	-	4	4-7	-	5	6-8	10-12	5
Rhinorrhea	<3	-	-	-	-	1-3	-	-
Sinusitis	-	-	-	≤1	-	-	4-5	≥2
Sneezing	4	-	-	-	-	-	-	-
Throat discomfort (burning, itching, swelling, pain)	-	Rare	-	-	-	Rare	-	-
Throat dryness/irritation	✔	Rare	-	-	-	Rare	-	-
Upper respiratory tract infection	-	-	-	-	-	-	5-7	-
Special senses								
Aftertaste	-	-	-	17	-	-	-	-
Blurred vision	-	-	-	-	-	✔	-	-
Cataracts	Rare	-	-	-	-	Rare	-	-
Conjunctivitis	-	-	-	-	-	✔	2-<5	-
Dry/irritated eyes	-	-	-	-	-	✔	-	-
Earache	-	-	2	-	-	-	2-<5	-
Glaucoma	Rare	-	-	-	-	Rare	-	-
Hoarseness	-	-	-	≤1	-	Rare	-	-
Increased intraocular pressure	Rare	Rare	-	-	-	Rare	Rare	-
Loss of taste/smell	Rare	Rare	-	≤1	-	✔	Rare	-
Otitis media	-	-	-	-	-	-	2-<5	≥2
Unpleasant taste/smell	✔	-	-	-	-	-	-	-
Watery eyes	<3	-	-	-	-	-	-	-
Miscellaneous								
Aches and pains	-	-	-	-	1	1-3	-	-
Arthralgia	-	-	-	-	-	-	2-<5	-

Adverse Events	Beclomethasone	Budesonide	Ciclesonide	Flunisolide	Fluticasone furoate	Fluticasone propionate	Mometasone	Triamcinolone
Chest pain	-	-	-	-	-	-	2-<5	-
Dysmenorrhea	-	-	-	-	-	-	1-5	-
Fever	-	-	-	-	4-5	1-3	-	-
Flu-like symptoms	-	-	-	-	-	1-3	2-<5	-
Growth suppression	✔	✔	-	-	-	✔	-	-
Infection	Rare	Rare	-	Rare	-	Rare	Rare	Rare
Myalgia	-	-	-	-	-	-	2-<5	-
Palpitations	-	Rare	-	-	-	-	-	-
Viral infection	-	-	-	-	-	-	8-14	-
Voice changes	-	-	-	-	-	Rare	-	-

✔ Percent not specified.
- Event not reported.

Contraindications/Precautions[4-11]

The use of intranasal corticosteroids in patients with a known hypersensitivity to any component of the preparation is contraindicated.

Several local nasal effects are associated with the use of intranasal corticosteroids, such as epistaxis, nasal ulceration, *Candida* infection, and nasal septal perforation. In addition, because of the inhibitory effect on wound healing, intranasal corticosteroids should be avoided in patients who have experienced recent nasal ulcers, nasal surgery, or nasal trauma until healing has occurred.

The development of glaucoma and/or cataracts may also result from the use of intranasal corticosteroids. Close monitoring is warranted in patients who experience a change in vision or who have a known history of increased intraocular pressure, glaucoma, or cataracts.

Due to the potential for worsening of infection, corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract, untreated local or systemic fungal or bacterial infections, systemic viral or parasitic infections, or ocular herpes simplex. Patients administering immunosuppressant doses of corticosteroids should avoid exposure to chickenpox and measles. Hypercorticism and adrenal insufficiency may appear in patients who administer higher than recommended doses of intranasal corticosteroids. If such changes occur, the dose of intranasal corticosteroid should be discontinued slowly, consistent with accepted procedure for discontinuing oral corticosteroid therapy. Also, if systemic corticosteroids are replaced with topical corticosteroids, signs of adrenal insufficiency and symptoms of corticosteroid withdrawal (i.e. joint and/or muscle pain, lassitude, and depression) may develop.

In addition, corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Growth should be routinely monitored in pediatric patients administering intranasal corticosteroids and the lowest dosage that effectively controls symptoms should be used.

Drug Interactions

Drug interactions associated with the use of intranasal corticosteroids are limited due to both the route of administration and the relatively low systemic bioavailability of the agents. There are no clinically significant drug interactions reported with beclomethasone, flunisolide, and triamcinolone. Since budesonide, ciclesonide, fluticasone furoate, fluticasone propionate, and mometasone are primarily metabolized in the liver by the cytochrome P450 3A4 (CYP3A4) isoenzymes systems, there are potential drug interactions with drugs that inhibit CYP3A4.

Table 7. Drug Interactions[12]

Generic Name	Interacting Medication or Disease	Potential Result
Budesonide ciclesonide, fluticasone furoate, fluticasone propionate, mometasone	Ketoconazole	Concurrent administration with ketoconazole, a potent inhibitor of CYP3A4, may increase the plasma concentration of budesonide, fluticasone furoate, fluticasone propionate, and mometasone. This may cause a decrease in plasma cortisol, resulting in adrenal suppression.
Fluticasone furoate, fluticasone propionate	Ritonavir	Fluticasone is metabolized by CYP3A4. Concurrent administration with ritonavir, a potent CYP3A4 inhibitor, may increase the plasma concentration of fluticasone and cause a decrease in plasma cortisol levels, resulting in adrenal suppression.

Dosage and Administration

Table 8. Dosing and Administration[4-11]

Generic Name	Adult Dose	Pediatric Dose	Availability
Beclomethasone	Nasal polyps, nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 42 to 84 µg (1 or 2 nasal inhalations) per nostril twice daily; maximum, 336 µg per day (administered as 2 nasal inhalations per nostril twice daily)	Nasal polyps, nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old: Suspension for nasal inhalation: initial, 42 µg (1 nasal inhalation) per nostril twice daily; maintenance, 42 to 84 µg (1 or 2 nasal inhalations) per nostril twice daily; maximum, 336 µg per day (administered as 2 nasal inhalations per nostril twice daily)	Suspension for nasal inhalation: 42 µg/inhalation (180 metered doses)
Budesonide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 32 µg (1 nasal inhalation) per nostril once daily; maximum, 256 µg per day (administered as 4 nasal inhalations per nostril once daily)	Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old: Suspension for nasal inhalation: initial, 32 µg (1 nasal inhalation) per nostril once daily; maximum, 128 µg per day (administered as 2 nasal inhalations per nostril once daily)	Suspension for nasal inhalation: 32 µg/inhalation (120 metered doses)
Ciclesonide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril once daily; maximum, 200 µg per day (administered as 2 nasal inhalations per nostril once daily)	Perennial allergic rhinitis in children ≥ 12 years old: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril once daily; maximum, 200 µg per day (administered as 2 nasal inhalations per nostril once daily) Seasonal allergic rhinitis in children ≥6 years old: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril once daily; maximum, 200 µg per day (administered as 2 nasal inhalations per nostril once daily)	Suspension for nasal inhalation: 50 µg/inhalation (120 metered doses)
Flunisolide	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 58 µg (2 nasal inhalations) per nostril twice daily; maintenance, 58 µg (2	Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 14 years old: Suspension for nasal inhalation: initial, 29 µg (1 nasal inhalation) per nostril	Suspension for nasal inhalation: 25 µg/inhalation (200 metered doses)

Generic Name	Adult Dose	Pediatric Dose	Availability
	nasal inhalations) per nostril two to three times daily; maximum, 464 µg per day (administered as 8 nasal inhalations per nostril per day)	three times daily or 58 µg (2 nasal inhalations) per nostril twice daily; maximum, 232 µg per day (administered as 4 nasal inhalations per nostril per day)	29 µg/inhalation (200 metered doses)
Fluticasone furoate	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 55 µg (2 nasal inhalations) per nostril once daily; maintenance, 27.5 µg (1 nasal inhalation) per nostril once daily	Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 11 years old: Suspension for nasal inhalation: initial, 27.5 µg (1 nasal inhalation) per nostril once daily; maximum, 110 µg per day (administered as 2 nasal inhalations per nostril once daily)	Suspension for nasal inhalation: 27.5 µg/inhalation (120 metered doses)
Fluticasone propionate	Nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal rhinitis: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril once or twice daily; maintenance, 50 µg (1 nasal inhalation) per nostril once daily	Nonallergic (vasomotor) rhinitis, perennial allergic rhinitis, seasonal rhinitis in children ≥ 4 years old: Suspension for nasal inhalation: initial, 50 µg (1 nasal inhalation) per nostril once daily; maintenance, 100 µg (1 nasal inhalations) per nostril once daily; maximum, 200 µg per day (administered as 2 nasal inhalations per nostril once daily)	Suspension for nasal inhalation: 50 µg/inhalation (120 metered sprays)
Mometasone	Nasal polyps in adults ≥18 years old: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril twice daily; maintenance, 100 µg (2 nasal inhalations) per nostril once daily Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 100 µg (2 nasal inhalations) per nostril once daily; maximum, 200 µg per day (administered as 2 nasal inhalations per nostril once daily)	Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 11 years old: Suspension for nasal inhalation: initial, 50 µg (1 nasal inhalation) per nostril once daily; maximum, 100 µg per day (administered as 1 nasal inhalation per nostril once daily)	Suspension for nasal inhalation: 50 µg/inhalation (120 metered doses)
Triamcinolone	Perennial allergic rhinitis, seasonal allergic rhinitis: Suspension for nasal inhalation: initial, 110 µg (2 nasal inhalations) per nostril once daily; maintenance, 55 µg (1	Perennial allergic rhinitis, seasonal allergic rhinitis in children 2 to 5 years old: Suspension for nasal inhalation: initial, 55 µg (1 nasal inhalation) per nostril	Suspension for nasal inhalation: 55 µg/inhalation (120 metered doses)

Generic Name	Adult Dose	Pediatric Dose	Availability
	nasal inhalation) per nostril once daily; maximum, 220 µg per day (administered as 2 nasal inhalations per nostril once daily)	once daily; maximum, 110 µg per day (administered as 1 nasal inhalation per nostril once daily) Perennial allergic rhinitis, seasonal allergic rhinitis in children 6 to 12 years old: Suspension for nasal inhalation: initial, 55 to 110 µg (1 or 2 nasal inhalations) per nostril once daily; maintenance, 55 µg (1 nasal inhalation) per nostril once daily	

Clinical Guidelines

Table 9. Clinical Guidelines

Clinical Guideline	Recommendations
Joint Task Force on Practice Parameters for Allergy and Immunology: **The Diagnosis and Management of Rhinitis: An Updated Practice Parameter (2008)**[1]	Diagnosis • An effective evaluation of a patient with rhinitis includes a determination of the pattern, chronicity, and seasonality of nasal and related symptoms; response to medications; presence of coexisting conditions; occupational exposure; and a detailed environmental history and identification of precipitating factors. • A physical examination with emphasis on the upper respiratory tract should be performed in patients with a history of rhinitis. • Skin testing is the preferred test for the diagnosis of IgE-mediated sensitivity and is indicated to provide evidence of allergic basis for the causes of the patient's symptoms. • Nasal smears for eosinophils are not necessary for routine use in diagnosing allergic rhinitis but may be useful when the diagnosis of allergic rhinitis is in question. • The measurement of total IgE should not be routinely performed. • Cytotoxic tests, provocation-neutralization, electrodermal testing, applied kinesiology, iridology, and hair analysis are not recommended diagnostic procedures. Treatment • The management and monitoring of rhinitis should be individualized and based on symptoms, physical examination findings, comorbidities, patient age and patient preferences. • Environmental control measures include avoidance of known allergic triggers when possible. • The available second-generation oral antihistamines, which are generally preferred over first-generation antihistamines, appear to be equally effective in the treatment of allergic rhinitis. • Concerning the second generation antihistamines, fexofenadine, loratadine, and desloratadine do not cause sedation at recommended doses; loratadine and desloratadine may cause sedation at doses exceeding the recommended dose; cetirizine and intranasal azelastine may cause sedation at recommended doses.

Clinical Guideline	Recommendations
	• Intranasal antihistamines are efficacious and equal to or superior to oral second-generation antihistamines for treatment of seasonal allergic rhinitis. • Intranasal antihistamines may be considered for use as first-line treatment for the treatment of allergic and nonallergic rhinitis. • Leukotriene receptor antagonists alone or in combination with antihistamines are effective in the treatment of allergic rhinitis. • Topical decongestants are not recommended for regular daily use but can be considered for short-term management of nasal congestion. • Intranasal corticosteroids are the most effective medication class for controlling symptoms of allergic rhinitis and all are considered equally efficacious. • Intranasal corticosteroids can provide significant relief of symptoms when used on a regular basis as well as an as-needed basis. • Intranasal corticosteroids may be useful in the treatment of some forms of nonallergic rhinitis. • A short course of oral corticosteroids may be appropriate for very severe or intractable nasal symptoms or significant nasal polyposis. • Intranasal cromolyn sodium may be effective for the prevention and treatment of allergic rhinitis. • Intranasal anticholinergics may be effective in reducing rhinorrhea and are more effective when used in combination with intranasal corticosteroids. • Allergen immunotherapy is effective and should be considered for patients with allergic rhinitis who have demonstrable evidence of specific IgE antibodies to clinically relevant allergens. • Surgery may be indicated in the management rhinitis.
Institute for Clinical Systems Improvement (ICSI): **Diagnosis and Treatment of Respiratory Illness in Children and Adults (2008)[3]**	Diagnosis • Patients can present with any of the following symptoms: congestion, rhinorrhea, pruritus, sneezing, posterior nasal discharge, and sinus pressure/pain. • A past medical history of facial trauma or surgery, asthma, rhinitis, atopic dermatitis, or thyroid disease may be suggestive of a rhinitis. In addition, a family history of atopy or other allergy associated conditions make allergic rhinitis more likely. • The most common physical findings suggestive of rhinitis tend to be swollen nasal turbinates, rhinorrhea and pruritus however allergic conjunctivitis may also be present. • Symptoms suggestive of allergic or episodic rhinitis include sneezing, itching of the nose, palate or eyes, and clear rhinorrhea. Nasal congestion is more commonly associated with perennial rhinitis. • Diagnostic testing should be considered if the results would change management. • Skin tests and radioallergosorbent tests identify the presence of IgE antibody to a specific allergen and are used to differentiate allergic from nonallergic rhinitis and to identify specific allergens causing allergic rhinitis. • A nasal smear for eosinophils can not differentiate allergic from nonallergic rhinitis. The test is a good predictor of a patient's response to treatment topical nasal corticosteroids. • Peripheral blood eosinophil count, total serum IgE level, Rinkel method of skin titration and sublingual provocation testing are not recommended.

Clinical Guideline	Recommendations
	Treatment • If a clinical diagnosis is obvious, symptomatic treatment, which consists of education on avoidance and medication therapy, should be initiated. • Avoidance of triggers is recommended. • Intranasal corticosteroids are the most effective single agents for controlling the spectrum of allergic rhinitis symptoms and should be considered first-line therapy in patients with moderate to severe symptoms. • Regular daily use of intranasal corticosteroids is required to achieve optimal results. • Systemic corticosteroids should be reserved for refractory or severe cases of rhinitis. Injectable steroids are not generally recommended. • Antihistamines are effective at controlling all symptoms associated with allergic rhinitis except nasal congestion. • Antihistamines are somewhat less effective than intranasal corticosteroids however oral antihistamines are an effective alternative in patients who cannot use or prefer not to use intranasal corticosteroids. They also can be added as adjunctive therapy to intranasal corticosteroids. • Second-generation antihistamines are recommended because they are less sedating and cause less central nervous system impairment. • Leukotriene inhibitors are as effective as second-generation antihistamines for the treatment of allergic rhinitis however are not as effective as intranasal corticosteroids. • Oral decongestants are effective in reducing nasal congestion. • Topical decongestants, which have the potential to induce rebound congestion after 3 days, are effective for the short-term relief of nasal congestion. • Cromolyn is most effective when used prior to the onset of allergic symptoms and is a good alternative to corticosteroids however four times daily dosing may cause compliance problems. • Intranasal anticholinergics are effective in relieving anterior rhinorrhea in allergic and nonallergic rhinitis. • Reserve immunotherapy for patients with significant allergic rhinitis in which avoidance activities and pharmacotherapy are insufficient to control symptoms. • If adequate relief is achieved appropriate follow-up should include further education on avoidance activities and medications. • If patients anticipate unavoidable exposure to known allergens they should begin the use of medications prior to exposure. • If adequate relief is not achieved within 2 to 4 weeks consider a trial of another medication, allergen skin testing by a qualified physician, a complete nasal examination, or a diagnosis of nonallergic rhinitis. • Treatment options for nonallergic rhinitis include intranasal corticosteroids, oral decongestants and antihistamines, topical antihistamines, and nasal strips.

Conclusions

Intranasal corticosteroids are used for the management of allergic rhinitis, some forms of nonallergic rhinitis, and nasal polyps. They are generally well tolerated and are associated with limited drug interactions. In addition, like other corticosteroids, intranasal corticosteroids carry warnings regarding the

use in patients with active infection and the development of signs of adrenal insufficiency with the administration of higher than recommended doses.

Intranasal corticosteroids are considered first-line agents for the treatment of allergic rhinitis; especially for patients with moderate to severe symptoms.[1,3] All available intranasal corticosteroids have demonstrated efficacy and safety.[13-56] These agents have been shown to be effective in reducing rhinitis-related nasal symptoms such as congestion, rhinorrhea, sneezing, nasal itch, and postnasal drip. The differences in tolerability and sensory perceptions noted in clinical trials were minor and did not translate to improved outcomes. Currently there are eight Food and Drug Administration (FDA) approved intranasal corticosteroids, two of which are available generically; flunisolide and fluticasone propionate. In addition, select intranasal corticosteroids are also FDA approved for the treatment of nasal polyps and nonallergic rhinitis.[4-6]

Nasacort Aqua® (triamcinolone), Nasonex® (mometasone), and Veramyst® (fluticasone furoate) are FDA approved for use in children ≥ 2 years old and the generic formulation of Flonase® (fluticasone furoate) is FDA approved for use in children ≥ 4 years old. All other intranasal corticosteroids, Beconase AQ® (beclomethasone), Rhinocort Aqua® (budesonide), Omnaris® (ciclesonide), and Nasarel® (flunisolide) are FDA approved for use in children ≥6 years old.

There is no substantial evidence that shows one intranasal corticosteroid to be more efficacious or safer than the other available intranasal corticosteroids. Therefore, all brand products within the class reviewed are comparable to each other and to the generic products in the class, and offer no significant clinical advantage over other alternatives in general use.

Recommendations

In recognition of the well established role of intranasal corticosteroids for the management of allergic rhinitis, nonallergic rhinitis, and nasal polyps and the lack of evidence supporting the use of one agent over another and cost considerations, no changes are recommended to the current approval criteria.

The following intranasal corticosteroids are preferred and are available without a prior authorization: fluticasone propionate, Nasacort AQ®, and Nasonex®.

Nonpreferred intranasal corticosteroids require prior authorization with the following approval criteria:

- The patient has had a documented side effect, allergy, or treatment failure to all three preferred nasal glucocorticoids. If a product has an AB rated generic, the generic must additionally be tried before approval of the brand.

In addition, quantity limits sufficient for a 30 day supply are in place for all preferred and nonpreferred intranasal corticosteroids.

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